

**What is Claimed:**

1. An isolated mammalian TGF $\beta$ -encoding nucleic acid comprising:
  - (a) a pro-TGF $\beta$  polynucleotide encoding a mammalian pro-TGF $\beta$  polypeptide, wherein the polynucleotide does not encode a cysteine residue within the first ten amino acid residues of the pro-TGF $\beta$  polypeptide; and
  - (b) a signal polynucleotide encoding a heterologous signal polypeptide, wherein the signal polynucleotide is in frame with the pro-TGF $\beta$  polynucleotide.
2. An isolated mammalian TGF $\beta$ -encoding nucleic acid according to claim 1 wherein the pro-TGF $\beta$  polynucleotide encodes a mammalian pro-TGF $\beta$  polypeptide comprising a mature TGF $\beta$  portion and a LAP portion, wherein the mature TGF $\beta$  portion is 95% identical to a mature human TGF $\beta$  molecule.
3. An isolated mammalian TGF $\beta$ -encoding nucleic acid according to claim 2 wherein the pro-TGF $\beta$  polynucleotide is selected from the group consisting of:
  - (a) a pro-TGF $\beta$  polynucleotide encoding a pro-TGF $\beta$  polypeptide, wherein the mature TGF $\beta$  portion is identical to mature human TGF $\beta$ 1;
  - (b) a pro-TGF $\beta$  polynucleotide encoding a pro-TGF $\beta$  polypeptide, wherein the mature TGF $\beta$  portion is identical to mature human TGF $\beta$ 2;
  - (c) a pro-TGF $\beta$  polynucleotide encoding a pro-TGF $\beta$  polypeptide, wherein the mature TGF $\beta$  portion is identical to mature human TGF $\beta$ 3;
  - (d) a pro-TGF $\beta$  polynucleotide encoding a pro-TGF $\beta$  polypeptide, wherein the mature TGF $\beta$  portion is identical to mature human TGF $\beta$ 1, and wherein the LAP portion is at least 90% identical to the LAP portion of human pro TGF $\beta$ 1;
  - (e) a pro-TGF $\beta$  polynucleotide encoding a pro-TGF $\beta$  polypeptide, wherein the mature TGF $\beta$  portion is identical to mature human TGF $\beta$ 2, and wherein the LAP portion is at least 90% identical to the LAP portion of human pro TGF $\beta$ 2; and
  - (f) a pro-TGF $\beta$  polynucleotide encoding a pro-TGF $\beta$  polypeptide, wherein the mature TGF $\beta$  portion is identical to mature human TGF $\beta$ 3, and wherein the LAP portion is at least 90% identical to the LAP portion of human pro TGF $\beta$ 3.
4. An isolated nucleic acid molecule according to claim 3, further comprising a tag polynucleotide encoding a purification tag polypeptide, wherein the tag polynucleotide is located between, and in frame with, the signal polynucleotide and the pro-TGF $\beta$  polynucleotide.

5. An isolated eukaryotic cell line comprising the isolated nucleic acid molecule of claim 4.
6. A vector comprising the isolated mammalian TGF $\beta$ -encoding nucleic acid molecule of claim 4.
7. An expression vector comprising the isolated mammalian TGF $\beta$ -encoding nucleic acid molecule of claim 4.
8. The expression vector of claim 7, wherein the nucleic acid is operatively linked to the regulatory sequence in an antisense orientation.
9. The expression vector of claim 8, wherein the polynucleotide is operatively linked to the regulatory sequence in a sense orientation.
10. A host cell comprising the nucleic acid of claim 4, or progeny of the cell.
11. The host cell of claim 10, which is a eukaryote.
12. The host cell of claim 11, wherein the nucleic acid is operatively linked to the regulatory sequence in an antisense orientation.
13. The polynucleotide of claim 4 that is RNA.
14. An isolated polypeptide encoded by a nucleic acid of claim 1.
15. The polypeptide of claim 14 that has the amino acid sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, or SEQ ID NO:4.
16. The isolated polypeptide of claim 14 that is fused with a heterologous peptide.
17. A method of producing mature TGF $\beta$  polypeptide comprising culturing an isolated eukaryotic cell line according to claim 5 in culture medium under conditions wherein greater than 25 mg of mature TGF $\beta$  per liter of culture medium is produced; and recovering the TGF $\beta$  polypeptide from the isolated cell line or its medium.
18. A method of producing mature TGF $\beta$  polypeptide comprising:
  - (a) culturing an isolated eukaryotic cell line according to claim 5 in culture medium under conditions to produce TGF $\beta$  complex in the culture medium, wherein TGF $\beta$  complex

comprises mature TGF $\beta$  polypeptide and LAP polypeptide fused with a purification tag polypeptide;

(b) purifying the TGF $\beta$  complex by binding the TGF $\beta$  complex with a binding agent that specifically binds the purification tag polypeptide;

(c) activating the TGF $\beta$  complex to dissociate mature TGF $\beta$  from associated LAP polypeptide; and

(d) separating mature TGF $\beta$  polypeptide from the LAP polypeptide; and

(e) recovering the TGF $\beta$  polypeptide from the isolated cell line or its medium.

19. A method of producing mature TGF $\beta$  polypeptide according to claim 18, wherein purified mature TGF $\beta$  is produced with a yield of greater than 15 mg per liter of culture medium and a purity of greater than 98%.

20. An isolated Chinese hamster ovary cell line comprising a pro-TGF $\beta$  polynucleotide encoding a mammalian pro-TGF $\beta$  polypeptide, wherein the polynucleotide does not encode a cysteine residue within the first ten amino acid residues of the pro-TGF $\beta$  polypeptide, or progeny of the cell line.

21. A method of producing mature TGF $\beta$  polypeptide comprising culturing an isolated eukaryotic cell line according to claim 20 in culture medium under conditions wherein greater than 25 mg of mature TGF $\beta$  per liter of culture medium is produced; and recovering the TGF $\beta$  polypeptide from the isolated cell line or its medium.

22. A method of producing mature TGF $\beta$  polypeptide comprising culturing an isolated eukaryotic cell line comprising a recombinant pro-TGF $\beta$  polynucleotide encoding a mammalian pro-TGF $\beta$  polypeptide, wherein the polynucleotide does not encode a cysteine residue within the first ten amino acid residues of the pro-TGF $\beta$  polypeptide, and wherein the cell line is cultured under conditions that produce greater than 25 mg of mature TGF $\beta$  per liter of culture medium; and recovering the TGF $\beta$  polypeptide from the isolated cell line or its medium.